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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,867	08/21/2001	Chaya Moroz	MOROZ3	6095

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EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/786,867

Applicant(s)

MOROZ, CHAYA

Examiner

MISOOK YU, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 67-83 is/are pending in the application.
- 4a) Of the above claim(s) 83 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 67-82 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> . |

Continuation of Attachment(s) 6). Other: Exhibits A-C (sequence alignments).

DETAILED ACTION

Election/Restrictions

Receipt of applicant's amendment filed on 01/31/2005 is acknowledged. All claims subjected to the Restriction mailed on 09/03/2004 are cancelled. Applicant states that newly presented claims 67-83 share a special technical feature. This argument has been fully considered but found unpersuasive for the reasons set forth below. New restriction of the pending claims is set forth below.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 67-82, drawn to a polypeptide, nucleic acid encoding said polypeptide, pharmaceutical comprising said polypeptide, expression vector, host cell, method of making said polypeptide, first method of using said polypeptide.

Group II, claim(s) 83, drawn to 2nd method of using the first claimed product.

The inventions listed as Groups I, and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to different categories are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said

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product; (2) A product and a process of use of said product; (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; (4) A process and an apparatus or means specifically designed for carrying out said process; or (5) A product, a process specially adapted for the manufacture of said product, and an apparatus or means specifically designed for carrying out said process.

If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group I will be the main invention. After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).) Group II invention above is 2nd method of using the product.

During a telephone conversation with Mr. Allen Yun on 04/12/2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 67-82. Affirmation of this election must be made by applicant in replying to this Office action. Claim 83 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 67-83 are pending. Claims 67-82 are examined on merits.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below. 37 CFR 1.821(a) presents a

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definition for "nucleotide and/or amino acid sequences." Nucleotide and/or amino acid sequences as used in 37 CFR 1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. Branched sequences are specifically excluded from this definition. Sequences with fewer than four specifically defined nucleotides or amino acids are specifically excluded from this section. "Specifically defined" means those amino acids other than "Xaa" and those nucleotide bases other than "n" defined in accordance with the World Intellectual Property Organization (WIPO) Handbook on Industrial Property Information and Documentation, Standard ST.25: Standard for the Presentation of Nucleotide and Amino Acid Sequence Listings in Patent Applications (1998), including Tables 1 through 6 in Appendix 2 (see MPEP § 2422).

The instant application contains an unbranched specifically defined sequence of more than ten nucleotides at pages 15, 19, and 27, Fig. 1-5, and 7. If those sequences are in the sequence listing, then inserting corresponding SEQ ID NO would obviate this objection to the specification. If any of those sequences is not listed in sequence listing, then new sequence listing, the corresponding CRF, and a new statement (i.e. the paper sequence listing, and CRF are same) are required.

Information Disclosure Statement

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application

specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609 subsection III. A(1) states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609 subsection III. C(1).

The information disclosure statement filed on 10/30/2001 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

Specification

The amendment filed 01/31/2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The Oath and Declaration filed on 03/21/2001 declares that the instant application is a 371 filed as PCT/IL 99/00485. However, SEQ ID NO:5 filed on 02/04/2005 and SEQ ID NO:5 disclosed in PCT/IL 99/00485 are not identical. Note Exhibit A (sequence alignment of SEQ ID NO:5 filed on 02/04/2005 and SEQ ID NO:5 disclosed in PCT/IL 99/00485).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 70, 77, 79, and 80 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 70 and 77 depend on claims 69, and 76 respectively, which in turn depend on claim 67, and 74 respectively. Claims 70, and 77 say that nucleotides 459-602 of SEQ ID NO:1 encode amino acid residues of 118-165 of SEQ ID NO: 5. However, the sequence alignment of SEQ ID NO: 5 with SEQ ID NO:1 (note Exhibit B) indicate that nucleotides 459-602 of SEQ ID NO:1 do not encode amino acid residues of 118-165 of SEQ ID NO: 5.

Claims 79, and 80 are objected because the parent claim 77 is drafted using the transitional phrase "consisting of", which means that the scope is limited to the recited part excluding any unrecited part. However, claims 79, and 80 are broadening the scope of its parent claim, because the claims include the part excluded by their parent claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 67-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has **two parts**.

First, this written description rejection is made because the claims 68-73 are interpreted as drawn to genus of products (proteins, nucleic acids, expression vectors, and hosts cells), and method of using said genus of products.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial sequence of residues of 118 to 165 of SEQ ID NO: 5. There is not even identification of any particular function associated with the partial sequence. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Second, claims 67-82 are rejected for a new matter. As noted above, SEQ ID NO:5 is a new matter. Applicant states that support for the new amendment is found at pages 12-14, 27-30, Figs 9, and 12. However, Figs. 9, and 12 are SDS-PAGE gel, and a diagram of effects of OFF1, respectively. The specification at pages 27-30 is about recombinant preparation of OFF1, and at page 27-30 about "OFF1". However, the specification as originally filed does not have support for "SEQ ID NO:5", "residues of 11 to 165 of SEQ ID NO:5", and "nucleotides of 459 to 602 of SEQ ID NO: 1". Further, the specification as originally filed does not have support for "arthritis" and "rheumatoid arthritis" in claims 81, and 82.

Claims 67-82 are rejected under 35 U.S.C. 112, first paragraph, as **failing to comply with the enablement requirement**. The claim(s) contains subject matter

which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There are two parts in this enablement rejection.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is Aundue≡ include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 67-82 are interpreted as drawn to a polypeptide, nucleic acid encoding said polypeptide, vector, host cell, method of making protein, and pharmaceutical for treatment of arthritis or rheumatoid arthritis and method of treating arthritis or rheumatoid arthritis, wherein the polypeptide and pharmaceutical comprises a polypeptide comprising amino acid residues of 118 to 165 of SEQ ID NO: 5, or a polypeptide consisting of amino acid residues of 118 to 165 of SEQ ID NO: 5.

The specification as originally filed does not teach how to make a protein comprising amino acid residues of 118 to 165 of SEQ ID NO: 5. Moroz et al., (J. Biol. Chem., Vol. 277, Issue 15, 12901-12905, April 12, 2002) are the first publication that discloses a protein sequence comprising amino acid residues of 118 to 165 of SEQ ID NO: 5. Note Exhibit C (a sequence alignment of SEQ ID NO:5 with the protein sequence disclosed at Fig. 1 at page 12902 of Moroz et al.). Moroz et al., was

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published three years after the instant application had been filed. Therefore, one of skill in the art would not know how to make a protein comprising or consisting of amino acid residues of 118 to 165 of SEQ ID NO: 5. As to the clinical uses of the newly discovered new human protein, Moroz et al., (some are inventor's of the instant application) concludes "With such characteristics, PLIF could become a therapeutic modality in high risk pregnancies associated with low levels or deficiency of PLF. Furthermore, PLIF and its active domain C48 may be developed into an immunosuppressive therapeutic factor for treatment of various immune-related disorders." This statement indicates that method of treating, especially rheumatoid arthritis.

In addition, Forre et al (2000, Scand J Rheumatol Vol. 29, pages 73-84) teach that rheumatoid arthritis is notoriously difficult to treat. See the entire article, especially 1st para, left column at page 81 for the general state of art for the treatment of rheumatoid arthritis using a similar approach as the invention claimed in the instant application and the first paragraph of the article, which states "Until the cause of rheumatoid arthritis (RA) is further elucidated, a successful prevention or repair of such tissue destruction remains elusive. This statement from the guidelines for the management of RA published by the American College of Rheumatology Ad Hoc Committee on clinical guidelines poses a major challenge to practicing rheumatologists and to the scientific community as a whole."

Considering the lack of sufficient guidance and/or working examples in the specification, and unpredictability in the art, and broad scope of claims as to the

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structural nature of the claimed products, it is concluded that undue experimentation is necessary to practice the invention.

Second, claims 72, and 79 are drawn to a host cell comprising the vector of previous claims, respectively. The claims are broadly interpreted to encompass host cells, which are not isolated and are comprised within an organism. Thus, the claims encompass host cells that have been transfected with the vector that are comprised within a transgenic animal, including nonhuman or human animals and animals treated using gene therapy.

The specification does not teach any method of overcoming technical difficulties that the art has been facing with the gene therapy. For example, Friedmann (Scientific American, June 1997, pages 96-101), Verma and Somia (1997, *Nature*, vol. 389, pages 239-242), and Rubanyi (2001, *Molecular Aspects of Medicine* 22, pages 113-142) all teach that gene therapy art still faces major hurdle to overcome. Rubanyi at the abstract teaches that the prerequisite of successful gene therapy includes "therapeutically suitable genes with a proven role in pathophysiology of the disease". The instant specification fails at this first prerequisite because the specification does not teach any therapeutically suitable genes with a proven role in pathophysiology of the disease. Friedman summarizes the current state of gene therapy as "treating disease by providing needed gene remains a compelling idea, but clinical and basic researchers still have much to do before gene therapy can live up to its promise" (note the italicized headline at the top of page 96). The instant specification does not teach a single technical problem being solved for gene therapy art. Verma et al. (*Nature* 1997, 389:

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239-242) teach that the Achilles heel of gene therapy is gene delivery. Verma et al. state that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression. Amending claims 72, and 79 to recite "isolated" before "host cell" would obviate these grounds of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off. Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Judy Ladrangan for Art Unit 1642 whose telephone number is 571-272-0536.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D

Examiner
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A handwritten signature in black ink, appearing to read "M. Smith", followed by a long, sweeping horizontal stroke.